SEQUENCE LISTING

<110> VLAAMS INTERUNIVERSITAIR INSTITUUT VOOR BIOTECHNOL <120> NOVEL INHIBITORS OF NF-kappaB ACTIVATION <130> 2676-4554US <140> 09/702,953 <141> 2000-10-31 <150> PCT/BE99/00055 <151> 1999-05-05 <150> US 09/702,953 <151> 2000-10-31 <150> 98201472.2 <151> 1998-05-06 <160> 19 <170> PatentIn version 3.2 <210> 1 <211> 2812 <212> DNA <213> Mus musculus <220> <221> Intron <222> (81)..(116) <220> <221> CDS <222> (117)..(2060) <400> 1 cacagggagg catggccgca ctcactgggc acatcttcag atcacctcgt gcattctcgg 60

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2.44	+~~	- cat		ממכ	· tat	: aca	aac	att	caa	aat	caq	ago	: tct	. caa	gtg	1991
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610	'				011	•										

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Glu Leu Val Lys Asp Ser Glu Leu Ser Pro Pro Thr Ser Ala Pro Ser 65 70 75 80

Leu Val Ser Phe Asp Asp Leu Ala Glu Leu Thr Gly Gln Asp Thr Lys
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Val Gln Val His Pro Ala Thr Ser Thr Ala Ala Thr Thr Thr Ala Thr
100 105 110

Ala Thr Thr Gly Asn Ser Met Glu Lys Pro Glu Pro Ala Ser Lys Ser 115 120 125

Pro Ser Asn Gly Ala Ser Ser Asp Phe Glu Val Val Pro Thr Glu Glu 130 135 140

Gln Asn Ser Pro Glu Thr Gly Ser His Pro Thr Asn Met Met Asp Leu

Gly Pro Pro Pro Glu Asp Ser Asn Leu Lys Leu His Leu Gln Arg 165 170 175

Leu Glu Thr Thr Leu Ser Val Cys Ala Glu Glu Pro Asp His Ser Gln
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Leu Phe Thr His Leu Gly Arg Met Ala Leu Glu Phe Asn Arg Leu Ala 195 200 205

Ser Lys Val His Lys Asn Glu Gln Arg Thr Ser Ile Leu Gln Thr Leu 210 225 220

Cys Glu Gln Leu Arg Gln Glu Asn Glu Ala Leu Lys Ala Lys Leu Asp 225 230 235 240

Lys Gly Leu Glu Gln Arg Asp Leu Ala Ala Glu Arg Leu Arg Glu Glu 245 250 255

Asn Thr Glu Leu Lys Lys Leu Leu Met Asn Ser Ser Cys Lys Glu Gly 260 265 270

Leu Cys Gly Gln Pro Ser Ser Pro Lys Pro Glu Gly Ala Gly Lys Lys 275 280 285

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Ala Lys Glu Leu Arg Gln Lys Val Arg Tyr Leu Gln Asp Gln Leu Ser 405 410 415

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Glu His Pro Pro Pro His Pro Asn Ser Arg Leu Phe His Leu Pro Glu 595 600 605

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<213> Mus musculus

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Asp Ser Glu Leu Ser Pro Pro Thr Ser Ala Pro Ser Leu Val Ser Phe 50 55 60

Asp Asp Leu Ala Glu Leu Thr Gly Gln Asp Thr Lys Val Gln Val His 65 70 75 80

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Ala Ser Ser Asp Phe Glu Val Val Pro Thr Glu Glu Gln Asn Ser Pro 115 120 125

Glu Thr Gly Ser His Pro Thr Asn Met Met Asp Leu Gly Pro Pro Pro 130 135 140

Pro Glu Asp Ser Asn Leu Lys Leu His Leu Gln Arg Leu Glu Thr Thr 145 150 155 160

Leu Ser Val Cys Ala Glu Glu Pro Asp His Ser Gln Leu Phe Thr His 165 170 175

Leu Gly Arg Met Ala Leu Glu Phe Asn Arg Leu Ala Ser Lys Val His 180 185 190

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Gln Arg Asp Leu Ala Ala Glu Arg Leu Arg Glu Glu Asn Thr Glu Leu 225 230 235 240

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Pro Ser Ser Pro Lys Pro Glu Gly Ala Gly Lys Lys Gly Val Ala Gly 260 265 270

Gln Gln Ala Ser Val Met Ala Ser Lys Val Pro Glu Ala Gly Ala 275 280 285

Phe Gly Ala Ala Glu Lys Lys Val Lys Leu Leu Glu Gln Gln Arg Met 290 295 300

Glu Leu Leu Glu Val Asn Lys Gln Trp Asp Gln His Phe Arg Ser Met 305 310 315

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Asp Leu Gln Lys Gln Val Thr Glu Leu Glu Ala Glu Arg Glu Gln Lys 340 345 350

Gln Arg Asp Phe Asp Arg Lys Leu Leu Leu Ala Lys Ser Lys Ile Glu 355 360 365

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Arg Gln Lys Val Arg Tyr Leu Gln Asp Gln Leu Ser Pro Leu Thr Arg 385 390 395 400

Gln Arg Glu Tyr Gln Glu Lys Glu Ile Gln Arg Leu Asn Lys Ala Leu 405 410 415

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Val Thr Gln Asn Glu Leu Leu Lys Gln Gln Val Lys Ile Phe Glu Glu 455

Asp Phe Gln Arg Glu Arg Ser Asp Arg Glu Arg Glu Arg Glu Arg 475

480

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Tyr Pro Pro Met Pro Ala Met Val Pro His His Ala Tyr Lys Asp Trp 545 550 555 560

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Pro His Pro Asn Ser Arg Leu Phe His Leu Pro Glu Tyr Thr Trp Arg
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Leu Glu Phe Asn Arg Leu Ala Ser Lys Val His Lys Asn Glu Gln Arg 130 135 140

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Ala Glu Arg Leu Arg Glu Glu Asn Thr Glu Leu Lys Lys Leu Leu Met 180 185 190

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Pro Glu Gly Ala Gly Lys Lys Gly Val Ala Gly Gln Gln Ala Ser 210 215 220

Val Met Ala Ser Lys Val Pro Glu Ala Gly Ala Phe Gly Ala Ala Glu 225 230 235 240 Asn Lys Gln Trp Asp Gln His Phe Arg Ser Met Lys Gln Gln Tyr Glu Gln Lys Ile Thr Glu Leu Arg Gln Lys Leu Val Asp Leu Gln Lys Gln Val Thr Glu Leu Glu Ala Glu Arg Glu Gln Lys Gln Arg Asp Phe Asp Arg Lys Leu Leu Ala Lys Ser Lys Ile Glu Met Glu Glu Thr Asp Lys Glu Gln Leu Thr Ala Glu Ala Lys Glu Leu Arg Gln Lys Val Arg Tyr Leu Gln Asp Gln Leu Ser Pro Leu Thr Arg Gln Arg Glu Tyr Gln Glu Lys Glu Ile Gln Arg Leu Asn Lys Ala Leu Glu Glu Ala Leu Ser 🦠 Ile Gln Ala Ser Pro Ser Ser Pro Pro Ala Ala Phe Gly Ser Pro Glu Gly Val Gly Gly His Leu Arg Lys Gln Glu Leu Val Thr Gln Asn Glu

Lys Lys Val Lys Leu Leu Glu Gln Gln Arg Met Glu Leu Leu Glu Val

Leu Leu Lys Gln Gln Val Lys Ile Phe Glu Glu Asp Phe Gln Arg Glu 405 410 415

Arg Ser Asp Arg Glu Arg Met Asn Glu Glu Lys Glu Glu Leu Lys Lys 420 425 430

Gln Val Glu Lys Leu Gln Ala Gln Val Thr Leu Thr Asn Ala Gln Leu
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Pro Glu His Val Cys Gly Ala Tyr Pro Tyr Ala Tyr Pro Pro Met Pro 485 490 495

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Pro Pro Pro Pro Val Pro Met Glu His Pro Pro Pro His Pro Asn Ser 515 520 525

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Val	Ile	Lys	Lys	Leu	Gln	Glu	Glu	Asn	Arg	Leu	Leu	Lys	Gln	Lys	Val	
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act	cat	gta	gaa	gac	ctc	aat	gct	aag	tgg	cag	cgt	tat	gat	gca	agt	784
Thr		Val	Glu	Asp	Leu	Asn	Ala	Lys	Trp	Gln	_	Tyr	Asp	Ala	Ser	
	220					225					230					
		-			_	999			-			-			_	832
Arg	Asp	Glu	Tyr	Val	Lys	Gly	Leu	His	Ala	Gln	Leu	Lys	Arg	Arg	Gln	

gtc	cct	ctg	gag	cct	gag	ctg	atg	aag	aag	gag	att	tcc	cga	ctt	aac	880
Val	Pro	Leu	Glu	Pro	Glu	Leu	Met	Lys	Lys	Glu	Ile	Ser	Arg	Leu	Asn	
				255					260					265		
aga	caq	ttg	gag	gag	aaa	ata	agt	gac	tgt	gcg	gaa	gca	aac	cag	gag	928
_	_					Ile						_		_	_	
5			270		-			275	-				280			
			2.4													
ctg	aca	gcc	atg	agg	atg	tcc	cgg	gac	act	gcg	ctg	gag	cga	gtg	cag	976
Leu	Thr	Ala	Met	Arg	Met	Ser	Arg	Asp	Thr	Ala	Leu	Glu	Arg	Val	Gln	
		285					290					295				
atq	cta	qaa	cag	cag	att	ctt	gct	tac	aag	gat	gac	ttc	aaa	tca	gaa	1024
_		-				Leu										
	300					305		_	_		310					
agg	qca	qat	cqq	qaa	cqa	gcg	cac	agt	agg	att	caa	gag	ctg	gag	gaa	1072
	_					Ala										
315		-			320					325					330	
320																
aaq	atc	atq	tcc	ttg	atg	tac	caa	gtg	tcc	cag	aga	cag	gac	tcc	cgg	1120
-		_		_	_	Tyr		-								
•				335		_			340					345		
gag	cca	qqa	ccc	tqt	caa	att	cat	acq	qqq	aac	aaa	act	gcc	aag	tac	1168
						Ile										
		1	350	-1-				355	•		•		360	•	-	
t.t.a	gag	atq	gat	aca	cta	gag	cat	ata	acc	cct	aac	aac	taa	agg	cct	1216
		_	-	_	_	Glu		-								
Dou	0_4	365	F				370				2	375	_	,		
		505					0.0									
gag	tot	add	tcc	caa	caq	atq	gaa	cct	tet	gca	gag	aat.	aaa	cat	gtg	1264
-					_	Met	_									
GIU		nr 9	DCL	. 0111	GIII	385	oru	110	DCI	1114	390		017	1110	• • • • • • • • • • • • • • • • • • • •	
	380					303					570					
+~~	262	~~~	~ ~~	262	ac+	a=~	~~+	as a	at t	a a a	taa	aat	cat	taa	cta	1312
_		-	_	_		cag		-								7777
Cys	Thr	Ala	GIn	Arg	GLY	Gln	GTÅ	Asp	ьeu	GIN	cys	Pro	nlS	cys	ьeu	

cgg tgc ttc agt gat gag caa ggc gag gca ttc ctc agg cac ctg tct

400

cgg tgc ttc agt gat gag caa ggc gag gca ttc ctc agg cac ctg tct
Arg Cys Phe Ser Asp Glu Gln Gly Glu Ala Phe Leu Arg His Leu Ser
415 420 425

1360

410

gag tgc tgc caa tga gccagacatt gcccgtgtga cccatgacca ccatagctgc 1415 Glu Cys Cys Gln

405

430

395

tctaagggac tgggaggggt cctcagactc agttttcaac tcagtgtgtt gcattctcct 1475 gggatctagg gcccaaatgg gcagggtcac tggaaggtca tcttgttttc atttgaccat 1535 ggtgagactt ggtcagaggg aactattgac agagcaggag gaagagggtg gggtcaggga 1595 1655 catcaagtgg acatcagttt tgtctcacgt agagtttgga gtgagctgtc aattcaaagc tgcaagctat cagttgtggg aatattctga agcctgcttg cacctagagt tatgccactt 1715 gctggaaggg gaagttgctg tgggagcagt gtgtcctctt tctagggtgg tagctccatc 1775 1835 ctgttgagta gtgagataca ctccctgact ggtctgtgct gcattacagt tacatgatac 1895 actagaacct teccaaacte ageagageea cacagetgea tecagtacea teaccetgea aaacacttgt atttccaaaa gggaaagcac ctttatttcc taatcattta tttttataat 1955 1967 aaatggcttt ac

<210> 6

<211> 430

<212> PRT

<213> Mus musculus

<400> 6

Met Ser Ser Gly Asp Pro Arg Ser Gly Arg Gln Asp Gly Ala Pro Arg

1 10 15

Ala Ala Ala Leu Cys Gly Leu Tyr His Glu Ala Gly Gln Gln Leu Gln Arg Leu Lys Asp Gln Leu Ala Ala Arg Asp Ala Leu Ile Ala Ser Leu Arq Thr Arq Leu Ala Ala Leu Glu Gly His Thr Ala Pro Ser Leu Val Asp Ala Leu Leu Asp Gln Val Glu Arg Phe Arg Glu Gln Leu Arg Arg Gln Glu Gly Ala Ser Glu Thr Gln Leu Arg Gln Glu Val Glu Arg Leu Thr Glu Arg Leu Glu Glu Lys Glu Arg Glu Met Gln Gln Leu Met Ser Gln Pro Gln His Glu Gln Glu Lys Glu Val Val Leu Leu Arg Arg Ser Val Ala Glu Lys Glu Lys Ala Arg Ala Ala Ser Asp Val Leu Cys Arg Ser Leu Ala Asp Glu Thr His Gln Leu Arg Arg Thr Leu Ala

Ala Thr Ala His Met Cys Gln His Leu Ala Lys Cys Leu Asp Glu Arg 165 170 175

Gln Cys Ala Gln Gly Asp Ala Gly Glu Lys Ser Pro Ala Glu Leu Glu Gln Thr Ser Ser Asp Ala Ser Gly Gln Ser Val Ile Lys Lys Leu Gln Glu Glu Asn Arg Leu Leu Lys Gln Lys Val Thr His Val Glu Asp Leu Asn Ala Lys Trp Gln Arg Tyr Asp Ala Ser Arg Asp Glu Tyr Val Lys Gly Leu His Ala Gln Leu Lys Arg Arg Gln Val Pro Leu Glu Pro Glu Leu Met Lys Lys Glu Ile Ser Arg Leu Asn Arg Gln Leu Glu Glu Lys Ile Ser Asp Cys Ala Glu Ala Asn Gln Glu Leu Thr Ala Met Arg Met Ser Arg Asp Thr Ala Leu Glu Arg Val Gln Met Leu Glu Gln Gln Ile

Ala His Ser Arg Ile Gln Glu Leu Glu Glu Lys Ile Met Ser Leu Met 325 330 335

Leu Ala Tyr Lys Asp Asp Phe Lys Ser Glu Arg Ala Asp Arg Glu Arg

Tyr Gln Val Ser Gln Arg Gln Asp Ser Arg Glu Pro Gly Pro Cys Arg 345 350 340 Ile His Thr Gly Asn Lys Thr Ala Lys Tyr Leu Glu Met Asp Ala Leu 360 365 355 Glu His Val Thr Pro Gly Gly Trp Arg Pro Glu Ser Arg Ser Gln Gln 370 375 380 Met Glu Pro Ser Ala Glu Gly Gly His Val Cys Thr Ala Gln Arg Gly 395 400 385 390 Gln Gly Asp Leu Gln Cys Pro His Cys Leu Arg Cys Phe Ser Asp Glu 405 410 415

Gln Gly Glu Ala Phe Leu Arg His Leu Ser Glu Cys Cys Gln
420 425 430

<210> 7

<211> 410

<212> PRT

<213> Mus musculus

<400> 7

Leu Cys Gly Leu Tyr His Glu Ala Gly Gln Gln Leu Gln Arg Leu Lys

1 10 15

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Leu Asp Gln Val Glu Arg Phe Arg Glu Gln Leu Arg Arg Gln Glu Glu Gly Ala Ser Glu Thr Gln Leu Arg Gln Glu Val Glu Arg Leu Thr Glu Arg Leu Glu Glu Lys Glu Arg Glu Met Gln Gln Leu Met Ser Gln Pro .90 . 85 Gln His Glu Gln Glu Lys Glu Val Leu Leu Arg Arg Ser Val Ala Glu Lys Glu Lys Ala Arg Ala Ala Ser Asp Val Leu Cys Arg Ser Leu Ala Asp Glu Thr His Gln Leu Arg Arg Thr Leu Ala Ala Thr Ala His Met Cys Gln His Leu Ala Lys Cys Leu Asp Glu Arg Gln Cys Ala Gln Gly Asp Ala Gly Glu Lys Ser Pro Ala Glu Leu Glu Gln Thr Ser Ser

Leu Ala Ala Leu Glu Gly His Thr Ala Pro Ser Leu Val Asp Ala Leu

Asp Ala Ser Gly Gln Ser Val Ile Lys Lys Leu Gln Glu Glu Asn Arg

Leu Leu Lys Gln Lys Val Thr His Val Glu Asp Leu Asn Ala Lys Trp 195 200 205

Gln Arg Tyr Asp Ala Ser Arg Asp Glu Tyr Val Lys Gly Leu His Ala 210 215 220

Gln Leu Lys Arg Arg Gln Val Pro Leu Glu Pro Glu Leu Met Lys Lys 225 230 235 235

Glu Ile Ser Arg Leu Asn Arg Gln Leu Glu Glu Lys Ile Ser Asp Cys 245 250 255

Ala Glu Ala Asn Gln Glu Leu Thr Ala Met Arg Met Ser Arg Asp Thr 260 265 270

Ala Leu Glu Arg Val Gln Met Leu Glu Gln Gln Ile Leu Ala Tyr Lys 275 280 285

Asp Asp Phe Lys Ser Glu Arg Ala Asp Arg Glu Arg Ala His Ser Arg 290 295 300

Ile Gln Glu Leu Glu Glu Lys Ile Met Ser Leu Met Tyr Gln Val Ser 305 310 315 320

Gln Arg Gln Asp Ser Arg Glu Pro Gly Pro Cys Arg Ile His Thr Gly 325 330 335

Asn Lys Thr Ala Lys Tyr Leu Glu Met Asp Ala Leu Glu His Val Thr 340 345 350

Pro Gly Gly Trp Arg Pro Glu Ser Arg Ser Gln Gln Met Glu Pro Ser 355 360 365

Ala Glu Gly Gly His Val Cys Thr Ala Gln Arg Gly Gln Gly Asp Leu 370 380

Phe Leu Arg His Leu Ser Glu Cys Cys Gln 405 410

<210> 8

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: consensus amino acid sequence
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<220>

<221> misc_feature

<222> (1)..(19)

<223> Xaa can be any amino acid

<400> 8

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Xaa Xaa Ser

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<210> 9
<211> 21
<212> PRT
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<220>
<221> misc_feature
<222> (1)..(21)
<223> Xaa can be any amino acid
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Leu Xaa Gln Gln Xaa Xaa Xaa Xaa Xaa Asp Phe Xaa Xaa Glu Arg
                                   10
                                                       15
                5
1
Xaa Asp Arg Glu Arg
            20
<210> 10
<211> 228
<212> PRT
<213> Mus musculus
<400> 10
Arg Gln Arg Glu Tyr Gln Glu Lys Glu Ile Gln Arg Leu Asn Lys Ala
                                    10
                                                        15
                5
Leu Glu Glu Ala Leu Ser Ile Gln Ala Ser Pro Ser Ser Pro Pro Ala
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25

20

Ala Phe Gly Ser Pro Glu Gly Val Gly Gly His Leu Arg Lys Gln Glu

35 40 45

Leu Val Thr Gln Asn Glu Leu Leu Lys Gln Gln Val Lys Ile Phe Glu 50 60

Glu Asp Phe Gln Arg Glu Arg Ser Asp Arg Glu Arg Met Asn Glu Glu 65 70 75 80

Lys Glu Glu Leu Lys Lys Gln Val Glu Lys Leu Gln Ala Gln Val Thr 85 90 95

Leu Thr Asn Ala Gln Leu Lys Thr Leu Lys Glu Glu Glu Lys Ala Lys
100 105 110

Glu Ala Leu Lys Gln Gln Lys Arg Lys Ala Lys Ala Ser Gly Glu Arg 115 120 125

Tyr His Met Glu Pro His Pro Glu His Val Cys Gly Ala Tyr Pro Tyr 130 135 140

Trp Ser Gln Ile Arg Tyr Pro Pro Pro Pro Val Pro Met Glu His Pro
165 170 175

Pro Pro His Pro Asn Ser Arg Leu Phe His Leu Pro Glu Tyr Thr Trp

180 185 190

Arg Pro Pro Cys Ala Gly Ile Arg Asn Gln Ser Ser Gln Val Met Asp 205 200 195 Pro Pro Pro Asp Arg Pro Ala Glu Pro Glu Ser Ala Asp Asn Asp Cys 220 210 215 Asp Gly Pro Gln 225 <210> 11 <211> 50 <212> DNA <213> Artificial Sequence <220> <223> Primer <400> 11 50 gaataccagg aggcgcagat ccagcggctc aataaagctt tggaggaggc <210> 12 <211> 35 <212> DNA <213> Artificial Sequence <220> <223> Primer <400> 12

31

gttgctgaaa gaggacgtca aaatctttga agagg

<210> 13 <211> 39

35 .

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                                                                    39 .
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<211> 62
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<213> Artificial Sequence
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<223> Primer
<400> 14
gcaggtaaaa atctttgaag aggacttcca gagggaacgg agtgatgcgc aacgcatgcc
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                                                                    62
cg
<210> 15
<211> 19
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: mutant ABIN-MUT1
<400> 15
Glu Tyr Gln Glu Ala Gln Ile Gln Arg Leu Asn Lys Ala Leu Glu Glu
                                                       15
                                   10
                5
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Ala Leu Ser

<210> 16 <211> 21 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: mutant ABIN-MUT2 <400> 16 Leu Lys Glu Glu Val Lys Ile Phe Glu Glu Asp Phe Gln Arg Glu Arg 10 5 Ser Asp Arg Glu Arg 20 <210> 17 <211> 21 <212> PRT <213> Artificial Sequence <220> <223> Description of Artificial Sequence: mutant ABIN-MUT3 <400> 17 Leu Lys Gln Gln Val Lys Ile Phe Glu Glu Asn Ala Gln Arg Glu Arg

Ser Asp Arg Glu Arg

5

20

<210> 18 <211> 21

1

10

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: mutant ABIN-MUT4

<400> 18

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1 5 10 15

Ser Asp Ala Gln Arg

20

<210> 19

<211> 594

<212> PRT

<213> Mus musculus

<400> 19

Met Glu Ala Ser Arg Leu Arg Gln Lys Ala Glu Glu Leu Val Lys Asp 1 5 10 10 15

Ser Glu Leu Ser Pro Pro Thr Ser Ala Pro Ser Leu Val Ser Phe Asp 20 25 30

Asp Leu Ala Glu Leu Thr Gly Gln Asp Thr Lys Val Gln Val His Pro

Ala Thr Ser Thr Ala Ala Thr Thr Ala Thr Ala Thr Thr Gly Asn 50 55 60

Ser Met Glu Lys Pro Glu Pro Ala Ser Lys Ser Pro Ser Asn Gly Ala

Ser Ser Asp Phe Glu Val Val Pro Thr Glu Glu Gln Asn Ser Pro Glu

Thr Gly Ser His Pro Thr Asn Met Met Asp Leu Gly Pro Pro Pro

Glu Asp Ser Asn Leu Lys Leu His Leu Gln Arg Leu Glu Thr Thr Leu

Ser Val Cys Ala Glu Glu Pro Asp His Ser Gln Leu Phe Thr His Leu

Gly Arg Met Ala Leu Glu Phe Asn Arg Leu Ala Ser Lys Val His Lys

Asn Glu Gln Arg Thr Ser Ile Leu Gln Thr Leu Cys Glu Gln Leu Arg

Gln Glu Asn Glu Ala Leu Lys Ala Lys Leu Asp Lys Gly Leu Glu Gln

Arg Asp Leu Ala Ala Glu Arg Leu Arg Glu Glu Asn Thr Glu Leu Lys

Lys Leu Leu Met Asn Ser Ser Cys Lys Glu Gly Leu Cys Gly Gln Pro

Ser Ser Pro Lys Pro Glu Gly Ala Gly Lys Lys Gly Val Ala Gly Gln

Gln Gln Ala Ser Val Met Ala Ser Lys Val Pro Glu Ala Gly Ala Phe 245 250 255

Gly Ala Ala Glu Lys Lys Val Lys Leu Leu Glu Gln Gln Arg Met Glu 260 265 270

Leu Leu Glu Val Asn Lys Gln Trp Asp Gln His Phe Arg Ser Met Lys 275 280 285

Gln Gln Tyr Glu Gln Lys Ile Thr Glu Leu Arg Gln Lys Leu Val Asp 290 295 300

Leu Gln Lys Gln Val Thr Glu Leu Glu Ala Glu Arg Glu Gln Lys Gln 305 310 315 320

Arg Asp Phe Asp Arg Lys Leu Leu Leu Ala Lys Ser Lys Ile Glu Met 325 330 335

Glu Glu Thr Asp Lys Glu Gln Leu Thr Ala Glu Ala Lys Glu Leu Arg 340 345 350

Gln Lys Val Arg Tyr Leu Gln Asp Gln Leu Ser Pro Leu Thr Arg Gln 355 360 365

Arg Glu Tyr Gln Glu Lys Glu Ile Gln Arg Leu Asn Lys Ala Leu Glu 370 375 380

Glu Ala Leu Ser Ile Gln Ala Ser Pro Ser Ser Pro Pro Ala Ala Phe

Gly Ser Pro Glu Gly Val Gly Gly His Leu Arg Lys Gln Glu Leu Val 405 410 415

385

Thr Gln Asn Glu Leu Leu Lys Gln Gln Val Lys Ile Phe Glu Glu Asp 420 425 430

Phe Gln Arg Glu Arg Ser Asp Arg Glu Arg Met Asn Glu Glu Lys Glu
435 440 445

Glu Leu Lys Lys Gln Val Glu Lys Leu Gln Ala Gln Val Thr Leu Thr 450 455 460

Asn Ala Gln Leu Lys Thr Leu Lys Glu Glu Glu Lys Ala Lys Glu Ala 465 470 475 480

Leu Lys Gln Gln Lys Arg Lys Ala Lys Ala Ser Gly Glu Arg Tyr His
485 490 495

Met Glu Pro His Pro Glu His Val Cys Gly Ala Tyr Pro Tyr Ala Tyr
500 505 510

Pro Pro Met Pro Ala Met Val Pro His His Ala Tyr Lys Asp Trp Ser 515 520 525

Gln Ile Arg Tyr Pro Pro Pro Pro Val Pro Met Glu His Pro Pro Pro 530 540

His Pro Asn Ser Arg Leu Phe His Leu Pro Glu Tyr Thr Trp Arg Pro

Pro Cys Ala Gly Ile Arg Asn Gln Ser Ser Gln Val Met Asp Pro Pro 565 570 575

Pro Asp Arg Pro Ala Glu Pro Glu Ser Ala Asp Asn Asp Cys Asp Gly 580 585 590

Pro Gln